## REMARKS

Favorable reconsideration is respectfully requested in view of the above amendments and following remarks. New claim 21 is drawn to the treatment of Alzheimer's disease or type 2 diabetes. The Examiner has indicated that a claim drawn to the treatment of type 2 diabetes or AD comprising the administration of an effective amount of the recited oligosaccharide would be allowable. Thus, claim 21 is allowable. New claim 22 is supported by the original disclosure, for example, at pages 16 and 17 of the specification. No new matter has been added. Claims 11-22 are pending.

### Claim Rejections- 35 U.S.C. 112

Claims 18 is rejected under 35 USC 112, first paragraph, because the specification does not provide enablement for the prevention of either type I or type II diabetes or the prevention of Alzheimer's disease (AD) or treatment for the full scope of oligosaccharides.

Applicants respectfully submit, as an Appendix, herewith supplementary experimental data establishing that the mannuronic acid oligosaccharide as recited in claim 18 can be used for the prophylaxis of Alzheimer's disease. The relevant experiments conducted are summarized as follows:

Experiment 1 provides *in vitro* experiments showing that the mannuronic acid oligosaccharide as recited in claim 18 can inhibit Aβ aggregation.

Experiment 2 provides experiments confirming the *in vitro* effects *in vivo* by using animal models of AD. Experiment 2 involves administering animal models of AD with the mannuronic acid oligosaccharide as recited in claim 18. Results showed statistically significant decrease in severity of brain legion formations that are diagnostic of AD.

Experiment 3 provides *in vivo* experiments showing that the mannuronic acid oligosaccharide as recited in claim 18 can preventively attenuate cognitive dysfunction in animals induced with Aβ.

The rejection refers to Doraiswamy et al. and indicates that actual cause of Alzheimer's disease remains a mystery and any potential surrogate biological markers for prevention have not been validated. However, work in the field of Alzheimer's diseases (AD) has identified a brain lesion that is diagnostic of AD, namely the senile (amyloid)

plaques (see, e.g., Selkoe, Trends in Cell Biology (Vol. 8), Nov., 1998; for the Examiner's convenience, a copy of the reference is enclosed). The major constituent of the extracellular amyloid plaques, which occurs in large numbers in brain areas important for memory and cognition, is the 40–42 residue amyloid β-protein (Aβ), a proteolytic fragment of the β-amyloid precursor protein (APP) (Id.). The end event of Aβ deposition is senile (amyloid) plaque formation, and thus, inhibition of Aβ aggregation prevents initiation of AD (Id.). Applicants have shown that the mannuronic acid oligosaccharide as recited in claim 18 can inhibit Aβ aggregation (see Experiment 1).

With regard to Experiment 2, double transgenic mice models with mutations in APP and presenilin 1 (PS1), another gene related to AD, have been shown to exhibit accelerated development of senile plaques and learning and memory deficits (see, e.g., Garcia-Alloza et al., Neurobiology of Diseases 24 (2006) 516-524; for the Examiner's convenience, a copy of the Garcia-Alloza et al. reference is enclosed). APP/PS1 double transgenic mice are generally accepted in the field of AD as animal models of AD (Id.), and exhibit one of the major pathological hallmarks of AD, which is the extracellular deposition of Aβ as dense-core or diffuse plaques (see, e.g., Pereson et al., J. Pathology 2009 219: 173-181; for the Examiner's convenience, a copy of the reference is enclosed). Applicants have shown that administering APP/PS1 double transgenic mice with the mannuronic acid oligosaccharide as recited in claim 18 results in a statistically significant decrease in one of the major pathological hallmarks of AD, that is, a statistically significant decrease in cerebral Aβ plaque burden and Aβ contents.

With regard to Experiment 3, escape latency in rats that were induced with Aβ1-140 were compared with escape latency in rats that were administered with the mannuronic acid oligosaccharide as recited in claim 18 before being induced with Aβ1-140. As shown in Figure 4 on page 8 of the Declaration, rats administered with the mannuronic acid oligosaccharide as recited in claim 18 exhibited shortened escape latency in a dose-dependent manner. The results in Experiment 3 show that the mannuronic acid oligosaccharide as recited in claim 18 can preventatively attenuate the cognitive dysfunction induced by Aβ1-140 in rats in a dose-dependent manner, and restore cognitive function to normal levels.

Applicants submit that the Experiments 1-3 provided in the Declaration establish that the mannuronic acid oligosaccharide as recited in claim 18 can be used for the prophylaxis of AD.

Moreover, Applicants respectfully submit that the supplementary experimental data establishes that the mannuronic acid oligosaccharide as recited in claim 18 can be used for the prophylaxis of diabetes. In particular, Experiment 4 of the Declaration provides experiments showing that the mannuronic acid oligosaccharide as recited in claim 18 can inhibit aggregation of amylin, which is a hallmark of type 2 diabetes.

In view of the above, Applicants submit that the Experiments 1-4 provided in the Declaration establish that the mannuronic acid oligosaccharide as recited in claim 18 can be used for the prophylaxis of Alzheimer's disease and diabetes. Withdrawal of the rejection is requested.

In view of the above amendments and remarks, Applicants believe that the pending claims are in a condition for allowance. Favorable reconsideration is respectfully requested. If any questions arise regarding this communication, the Examiner is invited to contact Applicants' representative listed below.

Respectfully submitted,



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